REMARKS

Claims 1-3 and 6-28 are pending. Claims 4-5 were previously cancelled. Claims 7-9, 13-14, 16-18, 24, and 26-27 are amended to delete the multiple dependency of said claims as originally presented in the preliminary amendment filed on April 16, 2001. Applicants respectfully submit that the claim amendments are in proper format and respectfully request entry of the amendment.

In response to the restriction requirement, wherein the Examiner required an election to one of the following groups of claims:

Group I, claims 1-3 and 6-13, drawn to an expression cassette encoding an insulin secretory signal operably linked to a sequence encoding somatotropin, cells having such an expression cassette, and a method of making somatotropin using such cells.

Group II, claims 14, 15 and 17-28, drawn to a capsule for implantation comprising cells comprising an expression cassette encoding an insulin secretory signal operably linked to a sequence encoding a somatotropin, and a method of administering somatotropin to a host using such a capsule.

Group III, claims 16, 18-20, draw to a method of administering somatotropin to a host comprising administering an expression cassette encoding an insulin secretory signal operably linked to a sequence encoding somatotropin.

Applicants hereby elect, with traverse, **Group I (claims 1-3 and 6-13)** for prosecution on the merits.

The Office Action at pages 2 and 3 asserts that the three groups of claims I-III do not relate to a "single general inventive concept" under PCT Rule 13.1 because, allegedly, under PCT Rule 13.2, they lack the same or corresponding special technical features. Although, the Office

Action identified a common technical feature of the groups, the "expression cassette encoding an insulin secretory signal operably linked to a sequence encoding somatotropin", the Office Action alleges that such special technical feature is not a contribution over the prior in view of the teachings of Cullen et al (1988) when combined with the teachings of O'Mahony et al. (1989). Applicants traverse the alleged lack of unity of invention over the alleged lack of inventive step for at least the following reasons.

Applicants respectfully submit that there is unity of invention. The special technical feature of the invention (i.e., an expression cassette encoding an insulin secretory signal operably linked to a sequence encoding somatotropin), contrary to the Office Action's assertion, does define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

In particular, the present invention is directed at increasing the **secretion** of a protein (i.e., somatotropin) whereas the Cullen et al. reference is directed at increasing the **expression** of a protein (i.e., interleukin 2). Cullen et al. in view of O'Mahony et al. do not teach or disclose the claimed invention of an expression cassette encoding in relevant part, an insulin secretory signal operably linked to a sequence encoding somatotropin. At best, Cullen et al. merely describes the **replacement of a portion of the 5' non-coding region of a native IL-2 cDNA** encoding the IL-2 protein secretory signal with a "leader element" derived from an efficiently translated gene, namely the rat preproinsulin II gene. Applicants submit that the "leader element" disclosed in Cullen et al. constitutes only **a portion of the rat preproinsulin II secretory signal**; in particular, a six (6) amino acid N-terminal portion of the rat preproinsulin II secretory signal (see Figure 1B of Cullen et al.).

Contrary to the Office Action's assertion, it is respectfully submitted that Cullen et al. does not disclose or suggest "expression vectors encoding an **insulin secretory signal** operatively linked to a heterologous protein". Applicants submit that protein secretory signals are typically 20 to 30 amino acids in length as disclosed in the claimed invention having an insulin secretory signal of 24 amino acids (See Figure 1.), and that it would not therefore be

expected that the 6 amino acid portion used by Cullen et al. would, on its own, bring about secretion of an operatively linked heterologous protein. In this regard, Applicants respectfully submit that Cullen et al. essentially retained all of the sequence encoding the native IL-2 protein secretory signal so that the secretion observed by Cullen et al. is the result of the IL-2's native secretory signal rather than the linkage of the 6 amino acid portion of the insulin secretory signal. (See page 647, first incomplete paragraph of the left hand column of Cullen et al., wherein it is indicated that the "insulin sequence replaced the IL-2 leader and sequences encoding the first two amino acids of the IL-2 signal peptide"). Contrary to the claimed invention (See Figures 1 and 2 of the application), Cullen et al. does not cleave and/or replace the native IL-2 protein secretory signal with an insulin secretory signal to achieve an increase in secretion of the somatotropin.

O'Mahony et al. (1989) fails to cure the deficiencies of Cullen et al. At best, O'Mahony et al. merely discloses three cDNA's encoding porcine somatotropin and the polymorphic characterization of those cDNAs. O'Mahony et al. does not disclose or suggest the possibility of replacing the somatotropin secretory signal with an insulin secretory signal so as to increase secretion of somatotropin from host cell.

Accordingly, it is submitted that persons of ordinary skill in the art would not arrive at the claimed invention by merely combining the teachings of the cited references. As such, Applicants respectfully request reconsideration and withdrawal of the restriction requirement and respectfully request examination on the merits of all the pending claims in this application.

CONCLUSIONS

Please grant any extension of time necessary for entry of this communication. Please charge any deficit fees, or credit any overpayment of fees, to Deposit Account No. 500417.

Respectfully submitted,

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